

EXHIBIT 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : PAOLETTI
U.S. Serial No. : 08/228,926
Filing Date : April 18, 1994
Title of the Invention : MODIFIED VACCINIA VIRUS AND METHODS FOR
MAKING AND USING THE SAME
Confirmation No. : 4171
Examiner : Mary Mosher
Art Unit : 1648

745 Fifth Avenue
New York, NY 10151

FILED VIA EFS

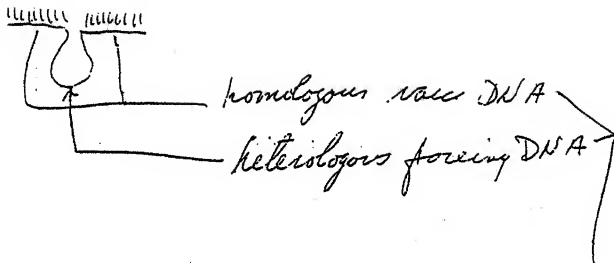
DECLARATION OF DR. ENZO PAOLETTI

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

ENZO PAOLETTI declares and states that:

1. I am a named inventor on the above-captioned application ("the present application"). I am familiar with the claims of the present application as pending.
 2. I submit herein a true copy of my handwritten notes from a date prior to the December 24, 1981 filing date of priority U.S. application Serial No. 06/334,456, which matured into U.S. Patent No. 4,769,330. The handwritten notes were authored solely by me in the United States. The handwriting in the handwritten notes is solely my handwriting.
 3. The handwritten notes evince my sole conception of the invention as claimed.
- Note especially the following in the attached:



4. In the above illustration, the handwriting is: "homologous vacc[inia] DNA" and "heterologous forei[gn] DNA".

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the application or any patent issuing thereon.

NOV. 15, 2008
Date


DR. ENZO PAOLETTI

EP has original

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August 27, 1980. It's a great beautiful day in New Hampshire. The sky is blue & the weather warm. These past few days have been really nice vacationing up here at Leo's. I hope the Volvo repairs won't cost too much. I checked the lab & received some of the most data ever than involved in an accident. The nuclear resonance experiments that Wilson began in the June have finally been moved and they are positive. It is possible to resolve sequences of inserted DNA with sufficient accuracy. The L and S variants have really proven to be very valuable in showing marker resonance. The donor DNA sequences are unique so there is no background as would be found with 15 reversions & deletions, due deletion, being able to cleave the donor DNA within or without the unique sequence allow for unequivocal data to be gathered. The ability to

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Demonstrate marker rescue will really be a boom to the molecular genetics of the phage, but there are potential applications of this basic technique that are just begging to be considered at this time. For example, we will now be able to manipulate the *Salmonella* genome by DNA recombination techniques and that one can now begin to seriously consider doing experiments such as:

- A) the construction of stable deletion mutants, i.e. specifically, adding the *Salmonella* genome of unnecessary DNA sequences and
- B) the insertion of "foreign DNA" into the *Salmonella* genome either at the deletion site that exists in the parent or the newer deletion that will be generated as per A above or by inserting foreign DNA at a number of restriction sites that are available and may be tailored for particular purposes. What we have

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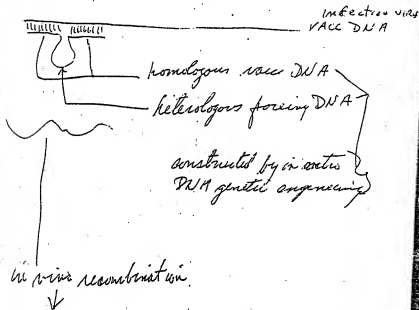
generated is a potentiated new cloning vector for foreign DNA by the exchange of in vitro DNA recombined as demonstrated by marker rescue. This new cloning vector, vaccinia virus, is unique consideration because it is so large in terms of DNA size, it is cytoplasmic in replication and has little danger of oncogenic considerations. The virus has been used successfully in the vaccination program leading to the eradication of smallpox. One of the most interesting purposes for using the new found virus is the construction of vaccines to various pathogenic organisms by insertion of the genetic information sequences (into the vaccinia genome) that are responsible for the synthesis of neutralizing antigens. Thus, as an example, it will be possible to insert into the vaccinia genome the DNA sequences from Hepatitis virus that

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are responsible for neutralizing herpes
infectivity. These antigens would
then be expressed after vaccine
infection and would result in
a vaccination against herpes.
The possibility of eliminating herpes 1
and herpes 2 which is a serious
problem and also implicated in
cervical carcinoma is quite
exciting. This is only a hypothesis,
and although the first approximation
to this new technology is admittedly
a simplistic one, there is no
reason to consider that it can not be
done. Its actuality appears to be only
a function of learning or applying
appropriate existing technology or
the modification or expansion of
vaccine DNA recombinant
technologies to this particular
problem. With sophistication
that comes with learning the
system it will be possible
to string a number of these
foreign DNA sequences together

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like a rosary such that one
vaccinia virus appropriately
manipulated can give rise to
a number of multilogging Abs
to a number of different pathogens like
a multivalent vaccination.



infectious vaccinia virus containing
a genome w/ a foreign DNA insert.

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There are a number of interesting questions of course that remain to be answered but their answers can undoubtedly be found in manipulation of the system.

For example - where in the vaccinia genome will a foreign DNA be expressed early/late - next to a strong weak vaccinia promoter - tandem repeats of foreign DNA inserts for amplification

The laboratory phase of this work will be very exciting and the potential applications of the discovery are overwhelming given this country's past